Shaine Morris

Dr. Kim Eagle: Hello, my name is Kim Eagle. I am the Hewlett Professor of Internal Medicine and one of the directors of the Frankel Cardiovascular Center at the University of Michigan. I also have the great privilege of being the study chair for an interesting study called the GenTAC Registry. It's a study sponsored by the National Heart, Lung, and Blood Institute looking at genetically triggered aortic conditions.

Today, I am talking to Dr. Shaine Morris. She's assistant professor of pediatrics in the section of cardiology at the Baylor College of Medicine.

Welcome, Shaine.

Dr. Shaine Morris: Thank you.

Dr. Eagle: We're delighted to have you as one of the investigators in GenTAC, and your work is absolutely fascinating, the studies that you're doing looking at kind of the morphology of the arteries in patients who have thoracic aortic disease. Start by telling us how you got interested in this area of arterial tortuosity.

Dr. Morris: Well, sure. I've always been interested in taking care of patients with genetic disorders. And so when I was doing my advanced imaging training in cardiac MRI I talked a lot with one of my mentors, Dr. Ronald Lacro, who is both a cardiologist and a geneticist. And I was trying to figure out a way to use imaging in helping improve care for these patients. And he had noticed a couple of his patients with Marfan Syndrome have a lot of vascular tortuosity on their MRIs, and that hadn't really be described. It had been known for a few years that we saw vascular tortuosity in Loeys-Dietz Syndrome, but hadn't really seen it in Marfan Syndrome and he sort of, we talked about looking and sort of describing this in other patients that had aortic disease. And first I had to come up with a method to measure it, and when I started looking really at patients we saw a lot of it and a variety of conditions and so then I asked to take the question further. Well is this actually associated with how they're going to do? Can we use this to predict how they're going to do and we had excellent results from examining that.

Dr. Eagle: So when an artery is tortuous, how do you actually, in a measurement sense, compare it to an artery that's not?

Dr. Morris: It's a great question, and even though people have noticed tortuosity for decades, it's never been quantified until now because that's hard to do. And so I looked at some other systems where people have looked at tortuosity of vessels and there's been something that sort of was described a long time ago when people looked at brain anatomy and we used something called the distance factor, but it's something very simple. So we basically measure, if you can imagine, if you have a long vessel that's sort of curled up or coiled or bendy, we can actually use 3-D pictures to measure the actual distance of the vessel in space and then we measure the distance that it should be, just from beginning to end, and we just take the ratio of those measurements. So if something, if you curl it up, it looks like it measures 9 centimeters but the straight line distance is only 6 centimeters, then we just do, you know 9 over six, and that excess length is the tortuosity.

Dr. Eagle: So you've created essentially an index comparing what would be considered a straight artery versus one that's twisted.

Dr. Morris: Exactly, so someone who has a straight artery might have two or three or five percent tortuosity, and a lot of our patients that have aortic disease can have 50 percent or 100 percent tortuosity.

Dr. Eagle: Wow, that's a big difference.

Dr. Morris: Yeah.

Dr. Eagle: Which arteries do you think might be useful in terms of measuring this in?

Dr. Morris: That's great, so what we noticed when we started looking at patient's MRIs, we sort of first started looking everywhere and saying "where do we see the most tortuosity?" and we do see some tortuosity in the carotid arteries which come off the aortic arch, but we saw most in the vertebral arteries. These are very, very small arteries that come off the vessels that come off the aortic arch that go to the brain. And they're quite small but they seem to be the most susceptible to tortuosity.

Dr. Eagle: Hmmm.

Dr. Morris: So, in our initial project we actually looked both at carotids and the vertebrals for the first 20 or 30 patients. But we saw significantly greater spread among the vertebral arteries and so we ended up using those as our main index and that's been what we continue to use.

Dr. Eagle: What do we know about what causes that twisting artery? What is the underpinning of that?

Dr. Morris: We don't 'really know, although we see that it's common in many different genetic mutations. And what we think, fundamentally, is that this is the artery lengthening when it's not supposed to, and it's lengthened in a fixed space between the heart and the brain. And because it's lengthening and has nowhere to go, it starts coiling on itself. And the thought is that in people with genetically mediated vascular disease, that somehow they're having abnormal adaptation to stress, either blood pressure or sort of perceived stress and so they lengthen as sort of a compensatory mechanism to that stress.

Dr. Eagle: I see, that's very interesting. It reminds me a little bit of the coronary arteries where we know when we develop a plaque, there's a remodeling process that the artery goes through and maybe this is an artery that's injured, trying to figure out what is the right shape.

Dr. Morris: Could be.

Dr. Eagle: Now I saw you present some very interesting research correlating tortuosity with outcomes. Tell our audience a little bit about that research.

Dr. Morris: Sure. So when we started looking at these patients, we wanted to know does this help us determine outcomes. And outcomes that are important in our population are how old are you when you have surgery, are you going to have an aortic dissection, is this associated with death, so we pick those as our first three outcomes. We also looked at frequency of surgery, how many surgeries per decade

you're going to need. And, so we look to see the patients with the highest VTI, the medium VTI, a VTI sorry is the vertebral artery tortuosity index, that is the index measurement, to see how it correlated with outcomes. So first we looked at age at first aortic surgery looking, sort of dividing the index into three groups. So what we saw is the most severely tortuous patients had the earliest age at surgery and their average first age at surgery was actually only 11 years old versus the patients with the lowest amount of tortuosity had a very late age at first surgery at 48 years old. So we saw a big difference in age at first surgery.

Dr. Eagle: And the patient cohorts were what, Marfan and…

Dr. Morris: These are mainly Marfan and Loeys-Dietz so it was 90 patients. There was 56 patients with Marfan Syndrome and 13 patients with Loeys-Dietz and the rest of them were patients who appeared to have a genetically mediated aortic disease but it hadn't been diagnosed with anything in particular but they had dismorphic, dismorphisms and they also had aortic disease.

Dr. Eagle: Ok.

Dr. Morris: So we looked… so then we looked at dissection and death. Now, we were looking in a young group of patients, so we didn't have that many people that had had aortic dissection or death, about 10 percent of the patients. And we saw that the index, the tortuosity index was strongly associated with earlier dissection and earlier death, as well.

Dr. Eagle: Wow.

Dr. Morris: Even when we controlled, even when we accounted for the size of their aorta. So, we noticed that the more tortuous you are, the bigger the aorta so we said, well, are we just coming up with another marker of severity that's the same as root size, the same as aortic size. But when we accounted for aortic size, it was still strongly predictive. So sort of a simpler way to say that is we took patients who had big aortas and little aortas and looked at how tortuous their vessels were and if you had a little aorta but high tortuosity your risk of early surgery and death was still high.

Dr. Eagle: So that's particularly important because it could be a new imaging marker of risk. We've used aortic size for a long time and we've known that it's imperfect and now your data could allow us a new imaging finding that could stratify patients and hopefully lead to changes in medical surveillance, therapy, and maybe even surgical cut points, I suppose.

Dr. Morris: That's exactly our goal, is to see if it can help sort of determine improved care on both sides of the spectrum. So connect those patients who don't have large aortas but are highly susceptible, maybe this is marker of patients who need earlier intervention. And on the other hand, patients who carry a genetic disorder that seems like they're highly susceptible to early dissection but if we can say it's protected, maybe we can reduce their imaging needs and defer their surgery til later.

Dr. Eagle: This is really very interesting. GenTAC is so fortunate to have young talented scientists like you involved in our work. And, on behalf of the audience of the GenTAC website, I want to thank you for taking time today.

Dr. Morris: Well thank you very much.